Warsaw breakage syndrome

Warsaw breakage syndrome is a condition that can cause multiple abnormalities. People with Warsaw breakage syndrome have intellectual disability that varies from mild to severe. They also have impaired growth from birth leading to short stature and a small head size (microcephaly). Affected individuals have distinctive facial features that may include a small forehead, a short nose, a small lower jaw, a flat area between the nose and mouth (philtrum), and prominent cheeks. Other common features include hearing loss caused by nerve damage in the inner ear (sensorineural hearing loss) and heart malformations.

Frequency

Warsaw breakage syndrome is a rare condition; at least four cases have been described in the medical literature.

Genetic Changes

Mutations in the *DDX11* gene cause Warsaw breakage syndrome. The *DDX11* gene provides instructions for making an enzyme called ChlR1. This enzyme functions as a helicase. Helicases are enzymes that attach (bind) to DNA and temporarily unwind the two spiral strands (double helix) of the DNA molecule. This unwinding is necessary for copying (replicating) DNA in preparation for cell division, and for repairing damaged DNA and any mistakes that are made when DNA is copied. In addition, after DNA is copied, ChlR1 plays a role in ensuring proper separation of each chromosome during cell division. By helping repair mistakes in DNA and ensuring proper DNA replication, the ChlR1 enzyme is involved in maintaining the stability of a cell's genetic information.

DDX11 gene mutations severely reduce or completely eliminate ChlR1 enzyme activity. As a result, the enzyme cannot bind to DNA and cannot unwind the DNA strands to help with DNA replication and repair. A lack of functional ChlR1 impairs cell division and leads to an accumulation of DNA damage. This DNA damage can appear as breaks in the DNA, giving the condition its name. It is unclear how these problems in DNA maintenance lead to the specific abnormalities characteristic of Warsaw breakage syndrome.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- WABS

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Warsaw breakage syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3150658/

Other Diagnosis and Management Resources

- Centers for Disease Control and Prevention: Hearing Loss in Children
  https://www.cdc.gov/ncbddd/hearingloss/
- MedlinePlus Encyclopedia: Hearing Loss--Infants
  https://medlineplus.gov/ency/article/007322.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Delayed Growth
  https://medlineplus.gov/ency/article/003021.htm
- Encyclopedia: Hearing Loss--Infants
  https://medlineplus.gov/ency/article/007322.htm
- Encyclopedia: Intellectual Disability
  https://medlineplus.gov/ency/article/001523.htm
- Health Topic: Growth Disorders
  https://medlineplus.gov/growthdisorders.html

Additional NIH Resources

- National Heart, Lung, and Blood Institute: What Are Congenital Heart Defects? https://www.nhlbi.nih.gov/health/health-topics/topics/chd/

Educational Resources

- Boys Town National Research Hospital: Types of Hearing Loss https://www.boystownhospital.org/knowledgeCenter/articles/hearing/Pages/TypesofHearing.aspx
- Centers for Disease Control and Prevention: Hearing Loss in Children https://www.cdc.gov/ncbddd/hearingloss/
- Centers for Disease Control and Prevention: Intellectual Disability https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/IntellectualDisability.pdf
- Cincinnati Children's Hospital: Short Stature https://www.cincinnatichildrens.org/health/s/short-stature
- Disease InfoSearch: Warsaw breakage syndrome http://www.diseaseinfosearch.org/Warsaw+breakage+syndrome/9470
- Johns Hopkins Children's Center: Short Stature http://www.hopkinsmedicine.org/healthlibrary/conditions/adult/pediatrics/short_stature_22,ShortStature/
- Kennedy Krieger Institute: Intellectual Disability https://www.kennedykrieger.org/patient-care/diagnoses-disorders/intellectual-disability
- MalaCards: warsaw breakage syndrome http://www.malacards.org/card/warsaw_breakage_syndrome
- Orphanet: Warsaw breakage syndrome http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=280558

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities (AAIDD) http://aaidd.org/
- American Heart Association http://www.heart.org/HEARTORG/
- Hearing Loss Association of America http://www.hearingloss.org/

- Hearing Loss Association of America
  http://www.hearingloss.org/
- The MAGIC Foundation
  https://www.magicfoundation.org/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28warsaw+breakage+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- WARSAW BREAKAGE SYNDROME
  http://omim.org/entry/613398

Sources for This Summary

- Capo-Chichi JM, Bharti SK, Sommers JA, Yammine T, Chouery E, Patry L, Rouleau GA, Samuels ME, Hamdan FF, Michaud JL, Brosh RM Jr, Mégarbane A, Kibar Z. Identification and biochemical characterization of a novel mutation in DDX11 causing Warsaw breakage syndrome. Hum Mutat. 2013 Jan;34(1):103-7. doi: 10.1002/humu.22226. Epub 2012 Oct 17.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23033317
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4599780/
- Wu Y, Sommers JA, Khan I, de Winter JP, Brosh RM Jr. Biochemical characterization of Warsaw breakage syndrome helicase. J Biol Chem. 2012 Jan 6;287(2):1007-21. doi: 10.1074/jbc.M111.276022. Epub 2011 Nov 18.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22102414
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3256869/
- van der Lelij P, Chrzanowska KH, Godthelp BC, Rooimans MA, Oostra AB, Stumm M, Zdzienicka MZ, Joenje H, de Winter JP. Warsaw breakage syndrome, a cohesinopathy associated with mutations in the XPD helicase family member DDX11/ChlR1. Am J Hum Genet. 2010 Feb 12;86(2):262-6. doi: 10.1016/j.ajhg.2010.01.008. Epub 2010 Feb 4.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20137776
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2820174/
- van der Lelij P, Oostra AB, Rooimans MA, Joenje H, de Winter JP. Diagnostic Overlap between Fanconi Anemia and the Cohesinopathies: Roberts Syndrome and Warsaw Breakage Syndrome. Anemia. 2010;2010:565268. doi: 10.1155/2010/565268. Epub 2010 Jul 18.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21490908
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3065841/

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/warsaw-breakage-syndrome

Reviewed: February 2014
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services